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Photochemical Synthesis of Anti-Isonicotinaldehyde Oxime

by

Edward J. Poziomek

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PHOTOCHEMICAL SYNTHESIS OF ANTI-ISONICOTINALDEHYDE OXIME

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Defensive Research Division
Directorate of Defensive Systems

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FOREWORD

This work was conducted under Project 1A01450'A91A, US Army Edgewood Arsenal Chemical Research and Development Laboratories In-House Laboratory Independent Research Program (U). The experimental data are contained in notebook 7136, pp 36-45. The work was performed during September 1964.

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DIGEST

Anti-isonicotinaldehyde oxime was prepared by irradiating an acetone solution of syn-isonicotinaldehyde oxime. This synthesis is convenient and simple and will for the first time allow various quaternary salts of the anti-isomer to be synthesized and their activities as therapeutic agents of anticholinesterase compounds to be determined.

It is concluded that this photolysis procedure may be applicable to the isomerization of other heterocyclic aldoximes and their quaternary salts.

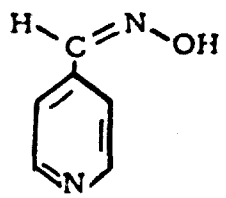
PHOTOCHEMICAL SYNTHESIS OF ANTI-ISONICOTINALDEHYDE OXIME

I. INTRODUCTION.

Quaternary salts of anti-isonicotinaldehyde oxime have not been examined as therapeutic agents in anticholinesterase poisoning because of the lack of a good method for synthesizing the anti-isomer. As a simple and convenient solution, this report describes the photochemical transformation of syn-isonicotinaldehyde oxime to the anti-isomer.

II. RESULTS.

Anti-isonicotinaldehyde oxime (I) has been isolated from an irradiation of syn-isonicotinaldehyde oxime. Previously, the anti-isomer has been prepared from isonicotinaldehyde and hydroxylamine in basic aqueous media at 10° to 15°C.[1] Slow titration with acetic acid resulted in the precipitation of (I). The procedure was not satisfactory, however, because of inconsistent reproducibility. Out of 10 runs, only 2 produced the anti-isomer, and then only in yields of less than 5%.[2]



(I)

The anti-isomer is prepared by irradiating a concentrated acetone solution of syn-isonicotinaldehyde oxime. Irradiation of a 15-ml acetone solution containing 1.2 gm of syn-isonicotinaldehyde oxime for 17 hr at 0° to 5°C in a 24/40 $\frac{T}{S}$ 13-mm ID tube fitted with an 8-in. quartz tube 2,537 Å lamp (Ultra-violet Products, Inc., San Gabriel, Calif.) resulted in the precipitation of crude (I). The syn-isonicotinaldehyde (mp 132° to 133°C) was used as obtained from Aldrich Chemical Co. One recrystallization from hot water gave 180 mg (15%) of a nearly colorless solid, mp 169° to 171°C (reported[1] 165° to 167°C). The configuration was confirmed by comparison of the nuclear-magnetic-resonance spectra of each isomer in deuterated methanol and acetone.[1] (These solvents are preferred over deuterated water because of the greater solubility of the anti-isomer.) Infrared absorption of the residue from an evaporated portion of the reaction solution indicated a mixture of anti- and syn-isomers. The experiment was repeated easily, but no attempt was made to increase the yield through longer irradiation times or by separation of the isomers left in solution.

The author believes that this is the first report of the photochemical isomerization of a pyridinecarboxaldehyde oxime. Amin and De Mayo[3] irradiated isonicotinaldehyde oxime (undoubtedly the syn-isomer) in acetic acid with an 80-w Hanovia CH 3 lamp in a quartz immersion apparatus. The primary purpose was to test for the formation of amide. The authors did not find isonicotinamide and did not indicate geometrical isomerization.

A number of significant possibilities stem from the convenient and simple preparation of (I). Some of the best-known compounds capable of reaction with anticholinesterases are N-alkyl derivatives of syn-isonicotinaldehyde oximes.[4-6] The corresponding quaternary salts of anti-isonicotinaldehyde oxime can now be synthesized and their activities determined. Furthermore, the molecular complementarity theory on the reactivation of inhibited acetylcholinesterase advanced by Wilson[7] may now be studied more easily.

III. CONCLUSION.

It is concluded that this photolysis procedure may be applicable to the isomerization of other heterocyclic aldoximes and their quaternary salts.

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13 ABSTRACT

(U) The anti-isonicotinaldehyde oxime was prepared by irradiating a concentrated acetone solution of syn-isonicotinaldehyde oxime for 17 hr at 0° to 5°C. This simple, convenient photolysis procedure can be used to synthesize various quaternary salts of the anti-isomer and may be applicable to the isomerization of other heterocyclic aldoximes and their quaternary salts.

14. KEYWORDS

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Quaternary salts
Anti-isomer
Isomers
Acetone
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